Complete Summary

GUIDELINE TITLE

Practice parameter for the diagnosis and management of primary immunodeficiency.

BIBLIOGRAPHIC SOURCE(S)

Bonilla FA, Bernstein IL, Khan DA, Ballas ZK, Chinen J, Frank MM, Kobrynski LJ, Levinson AI, Mazer B, Nelson RP Jr, Orange JS, Routes JM, Shearer WT, Sorensen RU. Practice parameter for the diagnosis and management of primary immunodeficiency. Ann Allergy Asthma Immunol 2005 May;94(5 Suppl 1):S1-63. [530 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Joint Council of Allergy, Asthma and Immunology. Practice parameters for the diagnosis and management of immunodeficiency. Ann Allergy Asthma Immunol 1996 Mar;76(3):282-94.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Primary immunodeficiency disorders (humoral immunodeficiency, cellular immunodeficiency, combined immunodeficiency, phagocytic cell disorders, complement deficiencies)

GUIDELINE CATEGORY

Diagnosis
Management
Prevention

CLINICAL SPECIALTY

Allergy and Immunology
Family Practice
Internal Medicine
Pediatrics

INTENDED USERS

Health Care Providers
Health Plans
Managed Care Organizations
Physicians

GUIDELINE OBJECTIVE(S)

To provide the consultant allergist/immunologist with a practical guide for the clinical recognition and diagnosis of immunodeficiency, along with the general principles that guide management of these disorders

TARGET POPULATION

Infants, children, and adults with primary immunodeficiency (humoral, cellular, combined, complement, or phagocytic cell disorders)

INTERVENTIONS AND PRACTICES CONSIDERED

Assessment

General

1. Physical exam
2. Patient and family history

B-Cell Function

Screening Tests

1. Serum immunoglobulin levels
2. Serum specific antibody titers

Advanced Tests

1. Antibody response to booster immunization
2. Flow cytometry to enumerate B cells
3. In vitro immunoglobulin production in response to mitogen

4. In vitro immunoglobulin production in response to anti-CD40 and cytokines
5. Antibody response to immunization with Phi X174

Cellular Immune Function

Screening Tests

1. Flow cytometry to enumerate T cells and natural killer cells
2. Cutaneous delayed hypersensitivity

Advanced Tests

1. Enzyme assays (adenosine deaminase [ADA], purine nucleoside phosphorylase [PNP])
2. Fluorescent in situ hybridization (FISH) for 22q11 and 10p11 deletion
3. In vitro proliferative response to mitogens and antigens
4. Natural killer cell cytotoxicity
5. Cytokine production in response to mitogen or antigen stimulation
6. Expression of surface markers after mitogen stimulation

Phagocytic Cell Function

Screening Tests

1. Blood cell count with differential
2. Neutrophil staining, morphology

Advanced Tests

1. Oxidase function (dihydrorhodamine, nitroblue tetrazolium, chemiluminescence)
2. Flow cytometry for adhesion molecules
3. Chemotaxis
4. Phagocytosis
5. Enzyme assays (myeloperoxidase, glucose-6-phosphate dehydrogenase ((G6PDH))
6. White blood cell (WBC) turnover
7. Bacterial or fungal killing
8. Bone marrow biopsy

Complement Function

Screening Tests

1. CH_{50} (total hemolytic complement activity)
2. AH_{50} (alternative pathway hemolytic activity)

Advanced Tests

1. Level or function of individual complement components
2. Chemotactic activity of complement split products

Other

Advanced Tests

1. Molecular methods including Southern, Northern, and Western blots, polymerase chain reaction/single-strand conformational polymorphism (PCR/SSCP), DNA fingerprinting, and nucleotide sequencing

Management

1. Humoral immune deficiencies: Intravenous immunoglobulin (IVIG) replacement therapy; systemic antibiotics; avoidance of live viral vaccines; patient/parent education and genetic counseling; immunomodulators; splenectomy; chemotherapy; pneumococcal vaccines
2. Management of cellular immunodeficiencies: HLA-identical (sibling) bone marrow transplantation (BMT); subcutaneous interferon-gamma; antiviral therapy; antifungal agents; anti-mycobacterial therapy; avoidance of live viral vaccines; patient education and genetic counseling
3. Management of combined immunodeficiencies: BMT; splenectomy; antibiotic therapy; IVIG; cellular reconstitution; chemotherapy; antiviral prophylaxis; avoidance of live viral vaccines; avoidance of nonirradiated blood or products; avoidance of cytomegalovirus (CMV)-positive blood or cells; pneumocystis prophylaxis; polyethylene glycol-adenosine deaminase (PEG-ADA); anti-inflammatory therapy; granulocyte colony-stimulating factor (G-CSF); granulocyte macrophage colony-stimulating factor (GM-CSF); thymus transplantation; multidisciplinary care; gene therapy
4. Management of complement deficiencies: pneumococcal vaccine; meningococcal vaccine; immunomodulator therapy; antibiotic therapy
5. Management of phagocytic cell disorders: BMT; avoidance of live bacterial vaccines; antibiotic prophylaxis; interferon gamma; surgical or dental debridement; granulocytic transfusions; antifungals; G-CSF; fucose; chemotherapy; glucocorticosteroids

MAJOR OUTCOMES CONSIDERED

- Immune system function
- Prevention of infection
- Adverse effects of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Preparation of this Practice Parameter included a review of the medical literature, mainly via the PubMed database.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Ia Evidence from meta-analysis of randomized controlled trials

Ib Evidence from at least one randomized controlled trial

IIa Evidence from at least one controlled study without randomization

IIb Evidence from at least one other type of quasi-experimental study

III Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies and case-control studies

IV Evidence from expert committee reports or opinions or clinical experience of respected authorities or both

LB Evidence from laboratory-based studies

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Published clinical studies or reports were rated by category of evidence and used to establish the strength of the clinical recommendations.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

A. Directly based on category I evidence
B. Directly based on category II evidence or extrapolated from category I evidence
C. Directly based on category III evidence or extrapolated from category I or II evidence

D. Directly based on category IV evidence or extrapolated from category I, II, or III evidence
E. Directly based on category LB evidence
F. Based on consensus of the Joint Task Force on Practice Parameters

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A working group prepared the initial draft, which was subsequently reviewed by the Joint Task Force. The working draft of the Practice Parameter for the Diagnosis and Management of Primary Immunodeficiency was reviewed by several experts in allergy and immunology. These experts included reviewers appointed by the American College of Allergy, Asthma and Immunology (ACAAI) and American Academy of Allergy, Asthma and Immunology (AAAAI). The revised final document was approved by the sponsoring organizations and represents an evidence-based consensus parameter.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

This practice parameter includes algorithms for the initial evaluation and management of a patient with primary immunodeficiency accompanied by annotations (numbered to correspond to the algorithms). Guideline recommendations are presented in the form of summary statements. After each statement is a letter that indicates the strength of the recommendation. Grades of recommendations (A-F) and levels of evidence (Ia, Ib, IIa, IIb, III, IV, LB) are defined at the end of the Major Recommendations field.

Annotations to Algorithm 1: General Approach for the Diagnosis of Primary Immunodeficiency

1-1. The patient exhibits symptoms and signs consistent with primary immunodeficiency. It is assumed that immunosuppressive therapies and other medical conditions potentially resulting in secondary immunodeficiency and other anatomic or biochemical conditions potentially predisposing to infection either have been excluded or are not considered sufficient to explain the observed degree of infectious susceptibility.

1-2. Antibody deficiency is most frequently encountered and commonly presents with sinopulmonary bacterial infections. If these are the only types of infections under consideration, screening for antibody deficiency is appropriate.

1-3. Other forms of primary immunodeficiency may present with distinct infectious complications with or without sinopulmonary bacterial disease. Some of these forms of infection are more or less characteristic of specific categories of immunodeficiency (see Table 2 in original guideline document). Neisserial infections characterize terminal complement component deficiencies, abscesses and fungal pathogens are seen in phagocyte defects, and mycobacterial, disseminated, or opportunistic infections occur in cellular or combined deficiencies.

1-4. If the clinical presentation is consistent with severe combined immunodeficiency (SCID), then immediate referral for expedited evaluation and treatment (bone marrow transplantation [BMT]) is indicated.

1-5. Successful outcomes depend on timely intervention.

1-6. Suspected antibody deficiency may be evaluated according to Algorithm 2. Complement deficiency, phagocyte defects, and some combined deficiencies may have a clinical presentation similar to antibody deficiency and should be sought when there is not a definitive diagnosis of such. Depending on the clinical presentation, any of these could be an appropriate subsequent focus of investigation.

1-7. Suspected complement deficiency may be evaluated according to Algorithm 5.

1-8. Suspected phagocyte defects may be evaluated using Algorithm 4.

1-9. Suspected cellular or combined immunodeficiencies may be evaluated according to Algorithm 3.

1-10. Depending on the specific characteristics of the infections and other medical problems that occur in a given patient, one or all of these immune effector mechanisms may require evaluation. In some cases, no definitive immunologic defect is ascertained. These patients either have an undefined form of compromised immunity or some other medical problem predisposing them to infection.

1-11. Whenever possible, the evaluation and/or management of suspected primary immunodeficiency should be performed by, or in close consultation with, a clinician with experience in this area. At some time during evaluation or after diagnosis is established, referral should be made for further evaluation and/or guidance during therapy.

Annotations to Algorithm 2: Diagnosis of Humoral Immunodeficiency

2-1. The clinical presentation is primarily suggestive of an antibody defect or any evaluation of cellular function is so far normal, and the clinical presentation is at least consistent with a possible antibody deficiency. The initial laboratory examination of humoral immunity consists of measuring the levels of various immunoglobulin isotypes (IgG, IgA, IgM) in serum, as well as a measure of function, or specific antibody production.

2-2. Profound hypogammaglobulinemia with serum IgG levels less than 100 milligrams(mg)/dL in an infant or less than 2 to 3 grams(g)/L in an older child or adult should prompt additional evaluation of lymphocyte populations and cellular immune function (2-3) to investigate combined immunodeficiency (CID) and B-cell count.

2-4. Specific antibody responses may be impaired as a result of a B-cell defect or failure of T-cell help for antibody production, even if serum immunoglobulin levels are normal or near normal. This situation should also prompt evaluation of lymphocyte subsets and cellular immunity (2-3).

2-5. Cellular immunity is evaluated either because of severe hypogammaglobulinemia or impaired specific antibody production (or both). If cellular immunity is abnormal, then the eventual diagnosis will be a form of CID. If cellular immunity is normal, it is important to determine whether there appears to be a significant impairment of B-cell development (2-7).

2-6. There is no profound hypogammaglobulinemia or demonstrable impairment of specific antibody production. Is there any abnormality of serum immunoglobulins or IgG subclasses? Yes (2-8) or No (2-9).

2-7. Is B-cell count normal? Yes (2-10) or No (2-11).

2-8. All measurements are normal, and alternative explanations for recurrent infections should be sought.

2-9. Mild hypogammaglobulinemia in infants, low serum IgA or IgG subclasses, or other poorly defined immunoglobulin abnormalities may exist with normal levels of specific antibodies as measured by standard assays. Potential diagnoses include selective IgA deficiency (SIGAD), IgG subclass deficiency (IGGSD), or transient hypogammaglobulinemia (THI).

2-10. Hypogammaglobulinemia and/or impaired specific antibody formation are seen in common variable immunodeficiency (CVID), SIGAD, IGGSD, specific antibody deficiency (SAD), and some forms of hyper-IgM syndromes (HIM), such as activation-induced cytidine deaminase (AID) or uracil nucleoside glycosylase (UNG) deficiencies.

2-11. Hypogammaglobulinemia or agammaglobulinemia associated with low or absent B-cell counts is seen in X-linked agammaglobulinemia (XLA) or autosomal recessive agammaglobulinemia (ARA) and in CVID.

Annotations to Algorithm 3: Diagnosis of Cellular and Combined Immunodeficiencies

3-1. In this situation, it is appropriate to perform a complete screening evaluation of specific immune function, including measurement of immunoglobulin levels, specific antibody production, enumeration of lymphocyte subpopulations, evaluation of natural killer (NK) cell cytotoxicity, and measurement of T-cell function.

3-2. If the clinical and laboratory phenotype is consistent with SCID, every effort must be made to expedite definitive therapy (BMT). It is desirable to know the actual molecular defect, but this should not delay therapy.

3-3 through 3-14. The particular form of SCID may often be suspected based on the lymphocyte phenotype (see Table 5 in original guideline document). If T cells are present, their origin (mother or patient) should be determined.

3-4. If T cells are absent or only of maternal origin (3-6) and B cells are also absent, then one of the alymphocytic SCID syndromes should be considered (3-5). If B cells are present, along with NK cells (3-7), consider IL-7 receptor alpha (IL7RA) mutation or complete DiGeorge syndrome (DGS) (3-8).

3-9. If B cells are present but NK cells absent, consider mutations that involve common gamma chain, JAK3, or IL2RA.

3-10. If host T cells are present and there is selective depletion of $CD4^+$ cells, consider defects of major histocompatibility complex (MHC) class II expression (3-11).

3-12. If there is selective depletion of $CD8^+$ cells, consider defects involving MHC class I expression or ZAP70 deficiency (3-13).

3-14. Omenn syndrome is associated with a variable host T-cell phenotype, although there is not usually extreme preponderance of one cell type. One should also consider the possibility of a less common (possibly undefined) form of SCID or a severe phenotype of other CID, such as CD40 ligand (CD40L) deficiency.

3-15. If there is at least partial T-cell function, evaluation of NK cell cytotoxicity may partly guide the subsequent evaluation. It has been recently recognized that a few CID syndromes may be associated with depressed NK cytotoxicity. These include (but are not limited to) X-linked lymphoproliferative disease (XLP), nuclear factor of kappa B essential modifier (NEMO) deficiency and Wiskott-Aldrich syndrome (WAS) (3-16).

3-17. Whether NK function is abnormal or not, there may be characteristic clinical or laboratory features that may suggest a particular molecular diagnosis (see Table 3 in the original guideline document).

3-18. The clinical presentation and laboratory evaluation so far is suggestive of 1 or more particular disorders. Advanced molecular methods (see Table 4 in the original guideline document) may be applied to detect particular defects.

3-19. If there are no such distinguishing clinical or laboratory features or if the suspected diagnosis is proven incorrect, one should consider (3-20) an undefined CID, an atypical clinical presentation of a defined CID, or a severe presentation of a primary humoral immunodeficiency (3-21) (Algorithm 2).

Annotations to Algorithm 4: Diagnosis of Phagocyte Defects

4-1. The clinical presentation is primarily suggestive of a phagocyte defect or evaluation of other immune function is so far normal, and the clinical presentation is at least consistent with a possible phagocyte defect. A complete blood cell count with differential is necessary to show the absolute neutrophil count.

4-2. Marked leukocytosis is observed in most cases of leukocyte adhesion defects and should raise suspicion in the appropriate setting.

4-3. Defects associated with leukocyte adhesion deficiency (LAD) are readily screened by flow cytometry, which may establish the diagnosis (4-4).

4-5. Severe neutropenia may be associated with congenital agranulocytosis or cyclic neutropenia (4-6).

4-7. If leukocyte count is not abnormal and the clinical features are consistent, neutrophil oxidase function may be evaluated by dihydrorhodamine reduction, nitroblue tetrazolium, or chemiluminescence. Abnormal oxidase function is indicative of chronic granulomatous disease (CGD) (4-8).

4-9. Chediak-Higashi syndrome (CHS) and specific granule deficiency (SGD) are suspected based on clinical presentation and neutrophil appearance under microscopy.

4-10. In the absence of a known syndrome of phagocyte deficiency, it is necessary to establish a functional defect more precisely. These tests include assays of chemotaxis, adhesion, migration, and intracellular killing. If such a functional deficit is reproducible, then a diagnosis of a clinically defined or unspecified phagocyte defect may be considered (4-11). Hyper-IgE syndrome (HIES) is usually suspected based on the characteristic clinical presentation. If the presentation is not consistent with this or any of the above, another form of immunodeficiency should be sought (4-12).

Annotations to Algorithm 5: Diagnosis of Complement Deficiency

5-1. The clinical presentation is primarily suggestive of a complement deficiency or evaluation of other immune function is so far normal, and the clinical presentation is at least consistent with a possible complement deficiency. Two distinct algorithms are presented, depending on whether total hemolytic complement assay (CH_{50}) and alternative pathway hemolytic activity (AH_{50}) are measured sequentially (5a) or simultaneously (5b). The CH_{50} is available in many clinical laboratories; the AH_{50} is not so widely available (it is available from the Complement Laboratory of the National Jewish Medical Center, Denver, CO). Note that both will be normal in the setting of mannose-binding lectin (MBL) deficiency.

5a-2. Classical pathway function is measured first by the CH_{50}.

5a-3. Following determination of diminished classical pathway function, it is necessary to determine if there is complement consumption.

5a-4. More than one complement component level is diminished, indicating complement consumption. Another cause of immunodeficiency should be sought.

5a-5. A single complement component level or function is absent, indicative of deficiency of either an early classical pathway component or a terminal pathway component. Note that deficiency of factor H or factor I could lead to a diminished level of C3. The level of each component may be measured by enzyme-linked immunosorbent assay (ELISA), or function may be determined in a lysis assay.

5a-6. The CH_{50} is normal. If complement deficiency is still suspected, function of the alternative pathway is measured by the AH_{50}.

5a-7. Since it has already been determined that the CH_{50} is normal, isolated abnormal AH_{50} is indicative of a defect of a component of the alternative pathway. Each component may be measured by ELISA or functional assay.

5a-8. CH_{50} and AH_{50} are normal.

5b-2. CH_{50} and AH_{50} are measured at the same time.

5b-3. If both are abnormal, this may be due to complement consumption not a primary complement abnormality. Note that deficiency of factor H or factor I could lead to a diminished level of C3.

5b-4. Low levels of multiple complement proteins are indicative of consumption.

5b-5. If there is no complement consumption, simultaneous abnormality of CH_{50} and AH_{50} is indicative of a terminal pathway deficiency (i.e., C3, C5 to C9).

5b-6. If the CH_{50} is abnormal and AH_{50} is normal, this suggests a classical pathway component deficiency (C1, C2, C4) (5b-7).

5b-8. If the AH_{50} is abnormal and the CH_{50} is normal, this is indicative of a defect of a component of the alternative pathway (properdin, factor D) (5b-9). Note that homozygous deficiency of factor B has not been reported.

Annotations to Algorithm 6: General Considerations for Therapy of Primary Immunodeficiency

Four principal general categories of therapy are indicated: BMT or gene therapy, intravenous immunoglobulin (IVIG) or subcutaneous immunoglobulin (SCIG), antimicrobial prophylaxis for any pathogen to which the host is susceptible and for which preventive therapy is available, and immunization where appropriate (see Table 4 in original guideline document).

6-1. For SCID, BMT should be pursued as expeditiously as possible. IVIG or SCIG is indicated before BMT and as necessary afterward for persistent humoral immunodeficiency. (Note that the latter could be similar to either 6-2 or 6-3.) For some diseases, now or in the future, gene therapy is or may be a possibility.

6-2. For XLA, ARA, or CVID, IVIG or SCIG is appropriate at the time the diagnosis is established. Many also recommend routine initiation of antibacterial prophylaxis at this time. Some prescribe preventive antibiotics when IVIG or SCIG is inadequate for prevention of infection or when other conditions such as

bronchiectasis are present. Immunization may be considered, particularly with inactivated vaccines for which coverage by IVIG or SCIG is not reliable (e.g., influenza).

6-3. For milder antibody deficiencies (SIGAD, IGGSD, SAD), therapy is often initially with preventive antimicrobials and immunization. Depending on all of the clinical and laboratory features, IVIG or SCIG may be considered.

6-4. For specific cellular deficiencies or for non-SCID combined deficiencies, BMT is often considered. BMT may not be appropriate for milder forms or if a suitable donor is not available. Wherever there is significant impairment of specific antibody production (6-5), IVIG or SCIG should be given. Antimicrobial prophylaxis and immunization may also be appropriate, depending on the specific defect.

6-6. For some phagocyte defects (e.g., CGD), BMT should be considered. IVIG or SCIG is generally not appropriate for complement or phagocyte defects. Antimicrobial prophylaxis is essential for phagocyte defects and may be considered for complement deficiency. Immunization may be helpful.

Summary Statements

General Considerations

1. Individual immunodeficiencies are rare, but altogether they occur in more than 1 in 2,000 live births. (C)
2. Immunodeficiencies are classified according to the principal immunologic mechanisms that are disrupted. (D)
3. Antibody deficiency is the most common type of primary immunodeficiency. (C)
4. Immunodeficiency usually presents with signs and symptoms of infections that may be repetitive, severe, or refractory to therapy and caused by organisms of low virulence. (C)
5. It is critically important to confirm the precise focus of infection and organism whenever possible. (D)
6. Other conditions that may increase susceptibility to infection should be sought in patients with suspected immunodeficiency. (D)
7. The physician must exercise caution to rule out the possibility of secondary immunodeficiency underlying the patient's illness. (D)
8. Autoimmune diseases and malignancies are complications of many immunodeficiencies. (C)
9. Many immunodeficiency disorders have characteristic clinical features. (C)
10. The family history may be a critical diagnostic clue for the presence of immunodeficiency. (C)
11. A stepwise approach is used to evaluate suspected immunodeficiency. (D)
12. Evaluation of specific immune response is essential. (C)
13. Patients suspected of having a primary immunodeficiency require evaluation by a clinical immunologist with experience with these disorders. (D)
14. Wherever possible, immunodeficiency should be defined at the molecular genetic level. (D)
15. The possibility of an X-linked disease should be considered in female patients when other possibilities have been ruled out. (D)

16. Female carrier status should be determined for all potentially affected female relatives of male patients with X-linked immunodeficiencies. (D)
17. Following diagnosis, it is important to proceed quickly with preventive and/or replacement therapy. (C)
18. Immunodeficient patients often require more aggressive and prolonged antimicrobial therapy. (C)
19. Antibody replacement therapy is indicated for all disorders with significantly impaired antibody production. (B)
20. Antibiotics may be needed in addition to immunoglobulin replacement for preventing infection in antibody-deficient patients. (C)
21. Mild antibody deficiencies are treated initially with antibiotic prophylaxis. (C)
22. Immunoglobulin replacement therapy may be considered for milder forms of antibody deficiency where other therapies have failed or are not tolerated. (D)
23. The placement of permanent central venous access solely for the purpose of IVIG administration should be discouraged. (F)
24. A role for surgery in the prevention and treatment of infection in immunodeficient patients has not been established. (C)
25. Definitive therapy of cellular or CID requires reconstitution by hematopoietic stem cells. (C)
26. Only irradiated, cytomegalovirus (CMV)-negative, lymphocyte-depleted cellular blood products should be administered to patients with cellular immunodeficiency or CID. (C)
27. No live vaccines should be administered to patients with severely impaired specific immunity. (C)
28. Inactivated or subunit vaccines may be administered to immunocompromised patients. (C)
29. Frequent evaluation by a clinical immunologist with applicable experience is important for patients with immunodeficiencies. (D)
30. Education is important for optimal outcomes for patients and families with immunodeficiency. (D)

Humoral Immunodeficiencies

31. Most patients with XLA present with recurrent bacterial infections, particularly otitis media, sinusitis, and pneumonia, in the first 2 years of life. (C)
32. The physical examination of patients with XLA usually reveals absent lymph nodes and tonsils. (C)
33. Characteristic laboratory abnormalities of XLA include agammaglobulinemia and very low or absent B-cell counts. (C)
34. Bruton tyrosine kinase (BTK) protein is absent in most patients with XLA. (C)
35. Certain BTK mutations are associated with variant (milder) phenotypes. (C)
36. Antimicrobial agents are often required in addition to IVIG for therapy of XLA. (C)
37. Chronic enteroviral meningoencephalitis in XLA responds to treatment with high doses of IVIG and with the antiviral drug pleconaril. (C)
38. Lung transplantation has been performed successfully in patients with XLA. (C)
39. Symptoms, signs, laboratory abnormalities, and therapy of the agammaglobulinemias due to autosomal gene defects are generally identical to those of XLA. (C)

40. Prominent clinical features of AID or UNG deficiency include bacterial sinopulmonary infections, gastrointestinal infections, and lymphoid hyperplasia. (C)
41. Laboratory evaluation of humoral immunity in AID or UNG deficiency may reveal low IgG, IgA, and IgE levels together with elevated IgM levels. Specific antibody responses may be impaired. (C)
42. IVIG replacement therapy is indicated for all patients with AID or UNG deficiency. (C)
43. Inducible T-cell costimulator (ICOS) deficiency is characterized by recurrent respiratory tract bacterial infections and gastrointestinal infections. (C)
44. Patients with ICOS deficiency generally have panhypogammaglobulinemia and impaired specific antibody production, along with reduced B-cell counts. (C)
45. Absence of ICOS expression can be determined by flow cytometric methods. (C)
46. Gammaglobulin replacement and antimicrobial agents are the major elements of therapy for ICOS deficiency. (C)
47. The main clinical features of immunodeficiency, centromeric instability, and facial anomalies (ICF) syndrome include abnormal facies and respiratory tract infections. (C)
48. Immunologic abnormalities in ICF syndrome may include hypogammaglobulinemia and mild defects of T-cell function. (C)
49. Characteristic abnormalities of chromosomes 1, 9, and 16 are diagnostic of ICF syndrome. (C)
50. Gammaglobulin replacement is indicated for patients with ICF syndrome and hypogammaglobulinemia. (C)
51. The predominant clinical manifestations of CVID are recurrent upper and/or lower respiratory tract infections with encapsulated or atypical bacteria. (C)
52. Gastrointestinal tract disease is common in patients with CVID. (C)
53. Autoimmune diseases occur with increased frequency in patients with CVID. (C)
54. Nonmalignant lymphoproliferative disease is seen frequently in CVID. (C)
55. Hematologic and other malignancies occur with increased frequency in patients with CVID. (C)
56. Hypogammaglobulinemia and impaired specific antibody production are the hallmarks of CVID. (C)
57. T-cell abnormalities are frequently found in patients with CVID. (C)
58. Selected molecular genetic defects should be ruled out in patients who meet diagnostic criteria for CVID, whenever possible. (C)
59. CVID with thymoma may be a distinct syndrome (Good syndrome). (C)
60. Gammaglobulin replacement therapy and antimicrobial agents are the mainstays of therapy for CVID. (B)
61. Autoimmune, lymphoproliferative, or malignant diseases associated with CVID are treated as they would be in other clinical settings. (C)
62. In patients with Good syndrome, thymomas should be excised. (C)
63. SIGAD is defined as a serum IgA level of less than 0.07 g/L but normal serum IgG and IgM levels in a patient older than 4 years in whom other causes of hypogammaglobulinemia have been excluded. (C)
64. Clinical manifestations of SIGAD include respiratory and gastrointestinal tract infections, atopy, autoimmune diseases, and malignancy. (C)
65. Laboratory evaluation in SIGAD may reveal associated IGGSD and impaired specific antibody formation (C).
66. Atopic disease should be treated aggressively in patients with SIGAD. (C)

67. Aggressive antimicrobial therapy and prophylaxis are often indicated in patients with SIGAD. (C)
68. Rare patients with SIGAD may benefit from IVIG replacement therapy. (C)
69. IGGSD is defined as an abnormally low level of 1 or more IgG subclasses in patients with normal levels of total IgG and IgM; IgA level may also be low. (C)
70. The diagnosis of IGGSD is controversial. (D)
71. Some patients with IGGSD exhibit impaired specific antibody production. (C)
72. The major clinical association with IGGSD is recurrent sinopulmonary bacterial infection. (C)
73. IGGSD may be seen in a variety of primary and secondary immunodeficiencies and with a variety of additional clinical associations. (C)
74. The principles of management of IGGSD include therapy of allergy, preventive antibiotics, and cautious use of gammaglobulin in selected patients. (C)
75. The diagnosis of SAD should be considered in patients older than 2 years with recurrent upper and/or lower respiratory tract infections. (C)
76. SAD is characterized by normal concentrations of IgG, IgA, IgM, and IgG subclasses and abnormal IgG antibody responses to polysaccharide vaccines. (C)
77. Patients with SAD may benefit from additional immunization with conjugate pneumococcal vaccines. (C)
78. The clinical presentation of transient hypogammaglobulinemia (THI) is in infants and young children with recurrent bacterial sinopulmonary infections and frequent viral illnesses. (C)
79. In THI, immunoglobulin levels are below the age-specific normal range, specific antibody production is usually preserved, and cellular immunity is intact. (C)
80. Preventive antibiotic therapy may be indicated for patients with THI. A period of IVIG replacement may be considered. (C)
81. Any patient with primary hypogammaglobulinemia and normal cellular immunity who does not fulfill diagnostic criteria for the above disorders has hypogammaglobulinemia of an unspecified type. (D)
82. Management of unspecified hypogammaglobulinemia may include antimicrobial therapy and gammaglobulin replacement. (D)

Cellular Immunodeficiencies

83. Clinical manifestations of defects that involve the IFN-gamma/IL-12 axis are mainly diseases caused by bacille Calmette-Guerin (BCG) or other poorly pathogenic mycobacteria, disseminated tuberculosis, systemic and/or persistent nontyphi Salmonella, or severe herpesvirus infection. (C)
84. Standard screening measures of cellular and humoral immune function are normal in patients with defects of the IFN- gamma /IL-12 axis. (C)
85. Markedly increased serum IFN- gamma level can be used as a screening test to prompt further evaluation for IFN-gamma receptor (IFN- gamma R) defects. (C)
86. Individuals with partial IFN- gamma R mutations and IL-12 p40 or IL-12R beta 1 mutations with nontuberculous mycobacterial disease may benefit from adjunct therapy with subcutaneous interferon gamma. (C)
87. HLA-identical sibling BMT may be considered for therapy of IFN- gamma R mutation (C).

88. The principal clinical manifestations of chronic mucocutaneous candidiasis (CMCC) due to autoimmune regulator (AIRE) mutation are immune-mediated destruction of endocrine tissue, chronic candidiasis, and ectodermal dystrophy. (C)
89. Patients with clinical features consistent with AIRE mutation should be screened for this defect, when possible. (C)
90. Patients with AIRE mutation may benefit from immunosuppressive therapy. (C)
91. Patients with NK cell deficiency due to mutations of CD16 (Fc gamma RIII) may have severe or recurrent herpesvirus disease. (C)
92. Patients with isolated defects of cellular immunity who do not have mutations that affect the IFN-gamma/IL-12 axis should be screened for mutation in Fc gamma RIII by flow cytometry using anti-CD16 clone B73.1. (C)
93. Patients with recurrent disease caused by herpesviruses associated with FCGR3A mutation may benefit from specific chemoprophylaxis against herpesviruses. (C)
94. Acquired immunodeficiency syndrome (AIDS)-like opportunistic infections are often seen in individuals with idiopathic CD4 lymphocytopenia (ICD4L). (C)
95. Laboratory criteria for ICD4L include a $CD4^+$ T-cell count of less than 300 cells/mm^3 with no evidence of human immunodeficiency virus (HIV) or other retroviral infection by both serologic and molecular testing. (C)
96. Measurement of adenosine deaminase (ADA) activity should be considered in patients diagnosed as having ICD4L. (C)
97. Antimicrobial prophylaxis and IL-2 may be considered for therapy of ICD4L. (C)
98. Patients who present only with recurrent candidal infection of nails, skin, and mucous membranes should be considered for the diagnosis of CMCC. (C)
99. Laboratory abnormalities in CMCC may include defective cutaneous or in vitro T-cell response to Candida and low NK cell count and/or function. (C)
100. Antifungal agents are the mainstays of therapy for CMCC. (C)
101. Individuals with severe disease caused by herpesviruses or papillomaviruses who do not have another defined immunodeficiency should have phenotypic and functional assessments of NK cells performed. (C)
102. Patients with undefined NK cell defects may benefit from chemoprophylaxis against herpesviruses. (D)
103. Any patient with normal serum immunoglobulin levels and specific antibody production and evidence of impaired cellular immunity who does not fulfill clinical and laboratory diagnostic criteria for any of the above disorders may be considered to have a cellular immunodeficiency of an unspecified type. (D)
104. Therapy for unspecified cellular immunodeficiency must be individualized. (D)

Combined Immunodeficiencies

105. Patients with SCID present within the first few months of life with recurrent, persistent, or severe bacterial, viral, or fungal infections and failure to thrive, diarrhea, and rashes (C).
106. A suspicion of SCID should be considered an emergent condition. (C)
107. Physical examination reveals absence of lymphoid tissue and the thymus is radiographically undetectable. (C)

108. Characteristic laboratory abnormalities may include severe, age-adjusted lymphopenia and panhypogammaglobulinemia, 1 or more reduced or absent major lymphocyte subpopulations, and absent or profoundly reduced T-cell proliferation to mitogens and antigens. (C)
109. Some mutations in genes associated with SCID may lead to atypical (milder) phenotypes. (C)
110. Maternal T cells may engraft in some patients with SCID and obscure the peripheral blood lymphocyte phenotype. (C)
111. An established diagnosis of SCID should be considered a medical emergency. (C)
112. Patients with SCID may be immunologically reconstituted by BMT or gene therapy. (C)
113. Patients with SCID due to IL-2R gamma chain (common gamma chain) deficiency and ADA deficiency have been successfully treated with gene therapy. (C)
114. Patients with SCID or suspected SCID should receive gammaglobulin replacement therapy. (C)
115. Patients with SCID or suspected SCID should be protected from exposure to infectious agents. (C)
116. Patients with SCID or suspected SCID should receive prophylaxis for Pneumocystis carinii pneumonia (PCP). (C)
117. Early signs of infection should be promptly recognized, and antimicrobial regimens initiated early and for prolonged periods. (C).
118. Patients with SCID due to ADA deficiency may benefit from the administration of polyethylene glycol (PEG) ADA. (C)
119. The classic clinical expressions of WAS are X-linked inheritance, an eczematous skin eruption, petechiae, bruising or bleeding, and recurrent and severe infections, including opportunistic organisms, autoimmune diseases, and Epstein-Barr virus (EBV)-related B-cell lymphomas. (C)
120. Thrombocytopenia and small platelet size are the most characteristic laboratory abnormalities of WAS. (C)
121. Humoral immunologic abnormalities in WAS include dysgammaglobulinemia and impaired specific antibody production. (C)
122. Cellular immunologic abnormalities in WAS include T lymphocytopenia, impaired in vitro and in vivo T-cell responses, and decreased NK cell activity. (C)
123. A WAS protein (WASP) mutation is expressed in some female patients due to extreme nonrandom X-chromosome inactivation. (C)
124. WASP is measurable by Western blot or flow cytometry to establish a diagnosis. (C)
125. A molecular diagnosis should be established in every case of WAS for its prognostic value. (C)
126. The only curative therapy for WAS is BMT. (C)
127. Before BMT, WAS is managed by a combination of splenectomy, antibiotics, and gammaglobulin replacement. (C)
128. Gait ataxia, oculocutaneous telangiectasias, growth retardation, and immune deficiency are the most prominent and consistent clinical features of ataxia-telangiectasia (A-T). (C)
129. Immunologic abnormalities in A-T include low or elevated immunoglobulin levels, IgG subclass deficiencies, impaired specific antibody production, and alterations in lymphocyte populations. (C)
130. Cytogenetic abnormalities, such as chromosomal translocations and chromosome fragility, support a diagnosis of A-T and related disorders. (C)

131. Patients with A-T and related disorders experience an extreme susceptibility to ionizing radiation and radiomimetic drugs and have a high rate of cancer. (C)
132. Elevated levels of oncofetoproteins are highly characteristic of A-T but not related disorders. (C)
133. All children with persistent ataxia should have determination of serum alpha -fetoprotein (AFP) levels. (C)
134. A-T and related disorders should be considered in all children with persistent characteristic neurologic and/or cutaneous manifestations. (D)
135. Patients with A-T and related disorders benefit from a coordinated multidisciplinary approach to management. (D)
136. Antibiotic prophylaxis and/or gammaglobulin replacement therapy may be indicated for A-T and related disorders. (C)
137. Therapy of hematologic malignancy in A-T and related disorders should be administered by physicians with prior direct experience with this complication. (C)
138. Thymic dysplasia, cardiovascular structural defects, and hypoparathyroidism mark the triad of congenital defects in DiGeorge Syndrome (DGS). (C)
139. T-cell lymphopenia is the most common laboratory feature of DGS. (C)
140. Treatment of infants with complete DGS requires some form of cellular reconstitution. (C)
141. Patients with DGS require multispecialty care. (D)
142. Clinical features of CD40 and CD40L deficiencies include infections with viral, bacterial, fungal, and opportunistic pathogens and cytopenias. (C)
143. Immunologic abnormalities of CD40 and CD40L deficiencies affect both humoral and cell-mediated immunity. (C)
144. CD40L expression is most readily evaluated by flow cytometric methods on activated T cells. (C)
145. CD40 expression may be measured by flow cytometry on monocytes or B cells. (C)
146. Female patients with the HIM phenotype should be studied for CD40L mutation if CD40 mutation or other known autosomal recessive mutation associated with the HIM phenotype is not found. (C)
147. Prophylaxis for PCP is indicated for all patients with known or suspected CD40 or CD40L deficiency. (C)
148. Neutropenia in CD40 or CD40L deficiency should be treated with granulocyte colony-stimulating factor (G-CSF). (C)
149. BMT is curative for CD40L deficiency. (C)
150. Three characteristic phenotypes of XLP are fulminant infectious mononucleosis, lymphoma, and dysgammaglobulinemia. (C)
151. The immunologic findings in XLP are variable and depend on EBV exposure. (C)
152. Some patients with XLP have been diagnosed as having CVID. (C)
153. IVIG should be given to patients with XLP and hypogammaglobulinemia or dysgammaglobulinemia and infections. (C)
154. BMT can cure XLP. (C)
155. Patients with XLP and lymphoproliferative disease may be treated with chemotherapy followed by BMT. (C)
156. The warts, hypogammaglobulinemia, immunodeficiency, and myelokathexis (WHIM) syndrome is named for its cardinal clinical features. (C)

157. Laboratory findings in WHIM syndrome include neutropenia and variably depressed humoral and cellular immunity. (C)
158. IVIG replacement may reduce the rate of respiratory tract bacterial infections in WHIM syndrome. (C)
159. G-CSF and granulocyte-macrophage colony-stimulating factor (GM-CSF) increase neutrophil counts in patients with WHIM syndrome. (C)
160. The major clinical manifestations of defects in NF-kappa B regulation include ectodermal dysplasia and severe infections with viruses, bacteria, and atypical mycobacteria. (C)
161. Dysgammaglobulinemia and altered cellular immune function are observed in patients with defects of NF-kappa B regulation. (C)
162. Mycobacterial infection in patients with an IKBKG mutation should be treated with an aggressive antimicrobial regimen. (C)
163. Patients with IKBKG mutation should receive gammaglobulin replacement. (C)
164. Antimycobacterial and antiviral prophylaxis should be considered for patients with IKBKG mutation. (C)
165. Consider BMT for patients with defects of NF-kappa B regulation not infected with mycobacteria. (C)
166. The main clinical manifestation of IL-1R-associated kinase (IRAK-4) deficiency is serious infection with gram-positive bacteria. (C)
167. The results of screening tests of immune function are normal in patients with IRAK-4 deficiency. (C)
168. Defects of toll-like receptor (TLR) signaling are seen in IRAK-4 deficiency. (C)
169. Therapy in IRAK-4 deficiency is directed toward treatment and prevention of infection. (C)
170. Clinical features of caspase 8 deficiency include failure to thrive, respiratory tract bacterial infections, and viral infections. (C)
171. Laboratory features of caspase 8 deficiency include impaired pneumococcal vaccine response and relative CD4 lymphocytopenia. (C)
172. Management for caspase 8 deficiency is individualized. (D)
173. Any patient with abnormal serum immunoglobulin levels and/or specific antibody production and evidence of impaired cellular immunity who does not fulfill clinical and laboratory diagnostic criteria for any of the above disorders may be considered to have a CID of an unspecified type. (D)
174. Therapy for unspecified CID must be individualized. (D)

Phagocyte Defects

175. Deep-seated granulomatous infections with bacteria and fungi are characteristic of chronic granulomatous disease (CGD). (C)
176. The diagnosis of CGD may be established by measurement of phagocyte oxidase activity. (C)
177. Antimicrobial agents and interferon (IFN)-gamma reduce the rate of infections in patients with CGD. (A)
178. Granulocyte transfusions may be indicated for the treatment of infections in patients with CGD. (C)
179. In patients with CGD, aggressive surgical debridement is indicated for abscesses unresponsive to medical therapy. (C)
180. CGD may be cured by BMT. (C)

181. Partial oculocutaneous albinism and neurologic symptoms are characteristic of Chediak-Higashi syndrome (CHS). (C)
182. Giant azurophil granules are characteristic of neutrophils in CHS. (C)
183. Virtually all patients with CHS who do not die of infection eventually develop a lymphoproliferative disorder known as the accelerated phase. (C)
184. The accelerated phase may be treated with high-dose glucocorticosteroids and chemotherapeutic agents. (C)
185. BMT is curative for CHS, even in the accelerated phase. (C)
186. Clinical manifestations of Griscelli syndrome (GS) include pigmentary dilution, neurologic abnormalities, pyogenic infections, and a hemophagocytic syndrome. (C)
187. Most patients with GS have normal results on screening tests of immunodeficiency. (C)
188. The accelerated phase of GS should be treated with chemotherapy. (C)
189. GS is curable by BMT. (C)
190. Patients with leukocyte adhesion deficiency (LAD) type I or II present with cellulitis, abscesses, and bacterial and fungal respiratory tract infections. (C)
191. Delayed separation of the umbilical cord may be seen in LAD type I. (C)
192. A partial or moderate form of LAD type I has a milder clinical course. (C)
193. Characteristic facies, growth, and developmental delay and mental retardation are seen in LAD type II. (C)
194. Significant neutrophilia is almost always present in patients with LAD. (C)
195. LAD types I and II may be diagnosed by flow cytometric measurement of relevant phagocyte surface molecules. (C)
196. Therapy for LAD types I and II is supportive and dictated by aggressive prevention and management of infections. (C)
197. Fucose supplementation may ameliorate the course of LAD type II. (C)
198. BMT is curative of LAD type I. (C)
199. The main clinical manifestation of SGD is recurrent bacterial infections of the skin and respiratory tract. (C)
200. Microscopic examination of stained neutrophils can establish the diagnosis of SGD. (C)
201. Management of SGD is supportive. (C)
202. The clinical manifestations of neutropenia include bacterial respiratory tract and soft tissue infections, gingivostomatitis, and vaginal or rectal mucosal ulceration. (C)
203. Serial measurements of neutrophil counts are necessary to distinguish persistent from cyclic neutropenia. (C)
204. G-CSF may increase neutrophil counts. (C)
205. BMT may be curative for severe chronic neutropenia. (C)
206. The major clinical manifestations of hyper-IgE syndrome (HIES) include recurrent lung and skin infections and chronic dermatitis. (C)
207. Elevated serum IgE level and staphylococcus-binding IgE and eosinophilia are characteristic of HIES. (C)
208. The initial approach to therapy of HIES is directed toward management of its characteristic complications. (C)
209. The use of IVIG or IFN- gamma in HIES is controversial. (C)
210. BMT is not curative of HIES. (C)

211. Any patient with recurrent infections and a demonstrable isolated defect of phagocytic cell function who does not have any of the disorders above should be considered to have an unspecified phagocytic cell defect. (D)
212. Therapy for unspecified phagocytic cell dysfunction must be individualized. (D)

Complement Deficiencies

213. Total deficiencies of a complement protein are rare. (C)
214. Usually, hypocomplementemia results from complement component consumption caused by activation, as may occur in autoimmune disease or during infection. (C)
215. In general, absence of a component of the classical pathway of complement is associated with autoimmunity or frequent infection. (C)
216. Defects of the mannose-binding lectin (MBL) and the alternative complement activation pathways may be associated with increased susceptibility to bacterial infections. (C)
217. C3 deficiency is associated with high susceptibility to bacterial infections. (C)
218. Terminal pathway complement deficiencies are associated with susceptibility to neisserial infections. (C)
219. A patient with factor I deficiency may present with frequent infections and urticaria. (C)
220. Some patients with hemolytic uremic syndrome have abnormalities of the complement regulatory protein factor H. (C)
221. The rare deficiencies of numbered complement components can be detected with a laboratory test (CH_{50}). (C)
222. Alternative pathway complement function is measured by the AH_{50}. (C)
223. Immunization and antibiotic therapy are the major modes of treatment for complement deficiencies associated with recurrent infections. (C)
224. Anti-inflammatory therapies are indicated for treatment of autoimmune disease associated with complement deficiency. (C)

<u>Definitions</u>:

Category of Evidence

Ia Evidence from meta-analysis of randomized controlled trials

Ib Evidence from at least one randomized controlled trial

IIa Evidence from at least one controlled study without randomization

IIb Evidence from at least one other type of quasi-experimental study

III Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies and case-control studies

IV Evidence from expert committee reports or opinions or clinical experience of respected authorities or both

LB Evidence from laboratory-based studies

Strength of Recommendation

A. Directly based on category I evidence
B. Directly based on category II evidence or extrapolated from category I evidence
C. Directly based on category III evidence or extrapolated from category I or II evidence
D. Directly based on category IV evidence or extrapolated from category I, II, or III evidence
E. Directly based on category LB evidence
F. Based on consensus of the Joint Task Force on Practice Parameters

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for:

- General Approach for the Diagnosis of Primary Immunodeficiency
- Diagnosis of Humoral Immunodeficiency
- Diagnosis of Cellular and Combined Immunodeficiencies
- Diagnosis of Phagocyte Defects
- Diagnosis of Complement Deficiency
- General Considerations for Therapy of Primary Immunodeficiency

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each summary statement (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

The developers of this Practice Parameter hope to encourage wider recognition of primary immunodeficiency, increase uniformity and efficiency in evaluation, and enhance consistent application of specific diagnoses. Furthermore, it is hoped that improved understanding of the principles of management of these diseases will lead to better outcomes for these patients and their families.

POTENTIAL HARMS

Adverse effects of treatment: Acute and delayed adverse reactions to gammaglobulin preparations are detailed in the appendix of the original guideline.

CONTRAINDICATIONS

CONTRAINDICATIONS

Live vaccines are absolutely contraindicated in severely immunocompromised patients. Live vaccines should also be withheld from patients with milder immunodeficiency, because they have not been rigorously studied with respect to risk or benefit in this population.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This is a complete and comprehensive document at the current time. The medical environment is a changing environment, and not all recommendations will be appropriate for all patients. Because this document incorporated the efforts of many participants, no single individual, including those who served on the Joint Task Force, is authorized to provide an official American Academy of Allergy, Asthma, and Immunology (AAAAI) or American College of Allergy, Asthma, and Immunology (ACAAI) interpretation of these practice parameters. Any request for information about or an interpretation of these practice parameters by the AAAAI or ACAAI should be directed to the Executive Offices of the AAAAI, the ACAAI, and the Joint Council of Allergy, Asthma, and Immunology. These parameters are not designed for use by pharmaceutical companies in drug promotion. This parameter was edited by Dr Nicklas in his private capacity and not in his capacity as a medical officer with the Food and Drug Administration. No official support or endorsement by the Food and Drug Administration is intended or should be inferred.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Bonilla FA, Bernstein IL, Khan DA, Ballas ZK, Chinen J, Frank MM, Kobrynski LJ, Levinson AI, Mazer B, Nelson RP Jr, Orange JS, Routes JM, Shearer WT, Sorensen RU. Practice parameter for the diagnosis and management of primary immunodeficiency. Ann Allergy Asthma Immunol 2005 May;94(5 Suppl 1):S1-63. [530 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1995 Aug 31 (revised 2005 May)

GUIDELINE DEVELOPER(S)

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American College of Allergy, Asthma and Immunology - Medical Specialty Society
Joint Council of Allergy, Asthma and Immunology - Medical Specialty Society

GUIDELINE DEVELOPER COMMENT

These guidelines were developed by the Joint Task Force on Practice Parameters for Allergy and Immunology, which is sponsored by the American Academy of Allergy, Asthma, and Immunology, the American College of Allergy, Asthma, and Immunology and the Joint Council of Allergy, Asthma and Immunology.

SOURCE(S) OF FUNDING

Funded by the American Academy of Allergy, Asthma, and Immunology (AAAAI), the American College of Allergy, Asthma, and Immunology (ACAAI), and the Joint Council of Allergy, Asthma and Immunology (JCAAI).

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Joint Council of Allergy, Asthma and Immunology. Practice parameters for the diagnosis and management of immunodeficiency. Ann Allergy Asthma Immunol 1996 Mar;76(3):282-94.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Joint Council of Allergy, Asthma, and Immunology (JCAAI) Web site.

Print copies: Available from JCAAI, 50 N. Brockway, Ste 3-3 Palatine, IL 60067.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on October 1, 1998. The information was verified by the guideline developer on December 15, 1998. This NGC summary was updated by ECRI on August 19, 2005. The updated information was verified by the guideline developer on September 9, 2005.

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Date Modified: 9/25/2006